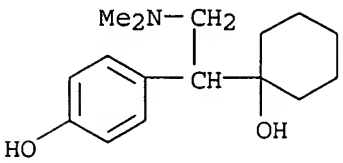
CAS ONLINE PRINTOUT

=> d l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 93413-62-8 REGISTRY
ED Entered STN: 18 Dec 1984
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-[2-(Dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol
CN Desvenlafaxine
CN DVS 233
CN **O-Desmethylvenlafaxine**
FS 3D CONCORD
DR 130198-07-1
MF C16 H25 N O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, HSDB*, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, MEDLINE, PHAR, PROMT, PROUSDDR, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

104 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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CAS ONLINE PRINTOUT

=> d his

(FILE 'HOME' ENTERED AT 08:53:40 ON 01 MAR 2006)

FILE 'REGISTRY' ENTERED AT 08:54:45 ON 01 MAR 2006
E O-DESMETHYLVENLAF/CN
L1 1 S E4

FILE 'CAPLUS' ENTERED AT 08:55:18 ON 01 MAR 2006
L2 104 S L1
L3 0 S L1/PUR
L4 10 S L1/P

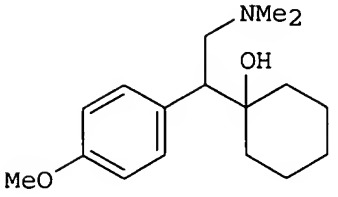
=> d bib abs 1-10

L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:759877 CAPLUS
DN 141:277347
TI Improved process for preparation of phenethylamine derivatives, particularly 1-(2-amino-1-phenylethyl)cycloalkanols useful as venlafaxine intermediates, by hydrogenation of corresponding nitriles over cobalt or nickel catalysts at controlled temperatures
IN Kim, Keun-sik; Kim, Kwang-il; Chai, Ki-byung
PA Wyeth, John, and Brother Ltd., USA
SO U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

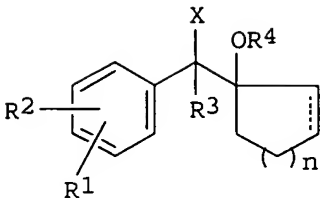
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004181093 | A1 | 20040916 | US 2004-797705 | 20040310 |
| | CA 2517164 | AA | 20040923 | CA 2004-2517164 | 20040309 |
| | WO 2004080934 | A2 | 20040923 | WO 2004-US7861 | 20040309 |
| | WO 2004080934 | A3 | 20041028 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1601640 | A2 | 20051207 | EP 2004-718880 | 20040309 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | NO 2005004300 | A | 20050930 | NO 2005-4300 | 20050916 |
| PRAI | US 2003-453583P | P | 20030311 | | |
| | WO 2004-US7861 | W | 20040309 | | |

OS CASREACT 141:277347; MARPAT 141:277347
GI

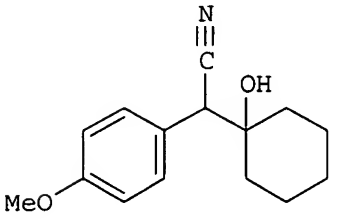
CAS ONLINE PRINTOUT



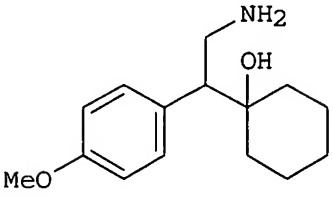

I




II




III




IV

AB An improved hydrogenation process for the preparation of certain drug intermediates is disclosed. The process is useful for the preparation of intermediates used in the manufacture of the antidepressant venlafaxine (I) and related compds. Specifically, the claimed process involves preparation of aminomethyl compds. II [X = CH2NH2] by hydrogenation of nitriles II [X = cyano] in the presence of a Ni or Co catalyst at a temperature of about 5° to about 25° [wherein: R1, R2 = (ortho or para substituents) H, OH, C1-6 alkyl, C1-6 alkoxy, C7-9 aralkoxy, C2-7 alkanoyloxy, C1-6 alkylmercapto, halo, or CF3; R3 = H or C1-6 alkyl; R4 = H, C1-6 alkyl, formyl, or C2-7 alkanoyl; n = 0, 1, 2, 3, or 4; dotted line = optional olefinic unsatn.]. The controlled temperature of the process prevents the formation of undesirable phenylalkylamine byproducts, which are typically formed at higher temps., and which are very difficult to sep. Also claimed is a process for alkylation of the obtained primary amines II [X = CH2NH2] to give secondary and tertiary amines II [X = NR5R6; R5 = H or C1-6 alkyl; R6 = C1-6 alkyl]. The latter compds. include I and various desmethyl derivs. For example, hydrogenation of nitrile III over Raney Ni in a mixture of MeOH and 25% NH3 solution, after 20-30 h at room temperature (10-20°) and 60 psi H2, gave amine IV in 70% yield and 99% purity, directly from the reaction. In contrast, a similar run at higher temps. (25°) gave IV of only 52% purity, with the major impurity (39% of product) being 4-MeOC6H4CH2CH2NH2. Alternatively, a too-low temperature run (5°) using more catalyst and NH3 was still incomplete at 45 h, and also gave IV of only 93% purity.

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:991300 CAPLUS
DN 140:47514
TI Novel formate salt of O-desmethyl-venlafaxine
IN Hadfield, Anthony Francis; Winkley, Michael William
PA Wyeth, John, and Brother Ltd., USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003103603 | A2 | 20031218 | WO 2003-US18195 | 20030609 |
| | WO 2003103603 | A3 | 20040325 | | |

CAS ONLINE PRINTOUT

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| | CA 2488613 | AA | 20031218 | CA 2003-2488613 | 20030609 |
| | US 2003236309 | A1 | 20031225 | US 2003-457596 | 20030609 |
| | US 7001920 | B2 | 20060221 | | |
| | BR 2003011693 | A | 20050322 | BR 2003-11693 | 20030609 |
| | EP 1519720 | A2 | 20050406 | EP 2003-757455 | 20030609 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | JP 2005533772 | T2 | 20051110 | JP 2004-510724 | 20030609 |
| | NO 2004005065 | A | 20050107 | NO 2004-5065 | 20041122 |
| PRAI | US 2002-387321P | P | 20020610 | | |
| | WO 2003-US18195 | W | 20030609 | | |

AB A novel salt of O-desmethylvenlafaxine, O-desmethylvenlafaxine formate, is provided. Pharmaceutical compns., dosage forms and methods of use are also provided.

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:435363 CAPLUS
DN 139:6675
TI Method and solvents for preparing O-desmethylvenlafaxine by the demethylation of venlafaxine with an alkane- or arenethiolate
IN Weber, Beat Theodor
PA Wyeth, John, and Brother Ltd., USA
SO U.S. Pat. Appl. Publ., 3 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2003105358 | A1 | 20030605 | US 2002-304871 | 20021126 |
| | US 6689912 | B2 | 20040210 | | |
| | CA 2466779 | AA | 20030612 | CA 2002-2466779 | 20021203 |
| | WO 2003048104 | A1 | 20030612 | WO 2002-US38403 | 20021203 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2002357049 | A1 | 20030617 | AU 2002-357049 | 20021203 |
| | BR 2002014701 | A | 20040831 | BR 2002-14701 | 20021203 |
| | EP 1451143 | A1 | 20040901 | EP 2002-804479 | 20021203 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| | JP 2005511681 | T2 | 20050428 | JP 2003-549297 | 20021203 |
| | US 2004158101 | A1 | 20040812 | US 2003-750196 | 20031231 |
| | NO 2004002680 | A | 20040625 | NO 2004-2680 | 20040625 |

PRAI US 2001-334953P P 20011204
US 2002-304871 A1 20021126
WO 2002-US38403 W 20021203
OS CASREACT 139:6675
AB O-desmethylvenlafaxine is prepared by reacting venlafaxine with a high-mol.-weight alkane- or arenethiolate anion (e.g., sodium dodecanethiolate) in an alc., ethylene glycol, polyethylene glycol (e.g., PEG 400), ethylene glycol ethers, or their mixts.

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:143294 CAPLUS
DN 136:189323
TI Preparation and pharmaceutical formulation of enantiomers of O-desmethyl venlafaxine
IN Yardley, John P.; Asselin, Andre A.
PA American Home Products Corporation, USA
SO U.S. Pat. Appl. Publ., 8 pp., Cont. of U.S. Ser. No. 590,741, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2002022662 | A1 | 20020221 | US 2001-957908 | 20010921 |
| | US 2002161055 | A1 | 20021031 | US 2002-154994 | 20020523 |
| | US 2003149112 | A1 | 20030807 | US 2003-373145 | 20030224 |
| | US 2004176468 | A1 | 20040909 | US 2004-799321 | 20040312 |
| | US 2005256206 | A1 | 20051117 | US 2005-183573 | 20050718 |
| PRAI | US 1999-183029P | P | 19990615 | | |
| | US 2000-590741 | B1 | 20000608 | | |
| | US 2001-957908 | A1 | 20010921 | | |
| | US 2002-154994 | B1 | 20020523 | | |
| | US 2003-373145 | A1 | 20030224 | | |
| | US 2004-799321 | B1 | 20040312 | | |

AB This invention provides pharmaceutically active enantiomers of the venlafaxine metabolite O-Desmethyl venlafaxine, R(-)-4-[2-(Dimethylamnino)-1-(1-hydroxycyclo-hexyl)ethyl]phenol or R(-)1-[2-(dimethylamino)-1-(4-hydroxyphenyl)ethyl]cyclohexanol (I), and S(+)-1-[2-(Dimethylamino)-1-(4-hydroxyphenyl)ethyl]cyclohexanol or S(+)-4-[2-(Dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol, or one or more pharmaceutically acceptable salts or salt hydrates thereof, as well as pharmaceutical compns. utilizing these enantiomers and methods of using the enantiomers to treat, inhibit or control central nervous system disorders. To a solution of 1-[2-(Dimethylamino)-1-(4-methoxyphenyl)ethyl]-cyclohexanol free base (preparation given) in EtOAc at room temperature was added at once to a solution of (+)-Di-para toluoyl-D-tartaric acid-monohydrate (DT(-)T) and was stirred at room temperature for 1 h. The resulting precipitate was filtered off, washed with EtOAc , dried overnight at 35° in a vacuum oven to provide crude R(-)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)-ethyl]cyclohexanol DT(-)T salt (yield = 92.8%) as a white solid. The solid was recrystd., and treated with sodium hydroxide solution to obtain I base which was separated and purified. Neurotransmitter uptake inhibition activity of the enantiomers were studied in rats. Pharmaceutical formulations of different enantiomers are disclosed.

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:900601 CAPLUS
DN 134:56475
TI Preparation and formulation of O-desmethyl venlafaxine enantiomers

CAS ONLINE PRINTOUT

IN Yardley, John Patrick; Asselin, Andre Alfred
PA American Home Products Corporation, USA
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000076955 | A1 | 20001221 | WO 2000-US16388 | 20000614 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI US 1999-183029P | P | 19990615 | | |
| US 1999-333594 | A | 19990615 | | |

AB Title compds. were prepared by optical resolution of venlafaxine followed by O-demethylation. Data for biol. activity of title compds. were given.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:384124 CAPLUS
DN 133:17270
TI Preparation of (-)-venlafaxine and derivatives as neuronal monoamine reuptake inhibitors.
IN Jerussi, Thomas P.; Senanayake, Chrisantha H.
PA Sepracor Inc., USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000032556 | A1 | 20000608 | WO 1999-US28303 | 19991201 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6342533 | B1 | 20020129 | US 1999-450690 | 19991130 |
| CA 2352324 | AA | 20000608 | CA 1999-2352324 | 19991201 |
| EP 1135359 | A1 | 20010926 | EP 1999-968056 | 19991201 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2003524613 | T2 | 20030819 | JP 2000-585198 | 19991201 |
| AU 774408 | B2 | 20040624 | AU 2000-24749 | 19991201 |
| US 2002086904 | A1 | 20020704 | US 2001-14592 | 20011214 |
| US 6441048 | B2 | 20020827 | | |
| US 2003018083 | A1 | 20030123 | US 2002-222815 | 20020819 |
| US 6911479 | B2 | 20050628 | | |
| US 2004180952 | A1 | 20040916 | US 2004-806423 | 20040323 |

CAS ONLINE PRINTOUT

PRAI US 1998-110488P P 19981201
US 1999-450690 A 19991130
WO 1999-US28303 W 19991201
US 2001-14592 A3 20011214
US 2002-222815 A3 20020819

AB A pharmaceutical composition comprising (-)-venlafaxine derivative substantially free of (+)-stereoisomer is claimed. Thus, (±)-venlafaxine in THF was added to a mixture prepared from Ph2PH and BuLi in THF at 0° followed by stirring and overnight reflux to give 73.8% (±)-O-desmethylvenlafaxine, which was resolved using di-p-toluoyl-L-tartaric acid to give (-)-O-desmethylvenlafaxine. Drug formulations containing the latter are given.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:384122 CAPLUS
DN 133:30575
TI Preparation of derivatives of (+)-venlafaxine as inhibitors of neuronal monoamine reuptake.
IN Jerussi, Thomas P.; Senannayake, Chrisantha H.
PA Sepracor Inc., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000032555 | A1 | 20000608 | WO 1999-US28306 | 19991201 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6197828 | B1 | 20010306 | US 1999-450691 | 19991130 |
| CA 2352321 | AA | 20000608 | CA 1999-2352321 | 19991201 |
| EP 1135358 | A1 | 20010926 | EP 1999-965065 | 19991201 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2003501344 | T2 | 20030114 | JP 2000-585197 | 19991201 |

PRAI US 1998-110486P P 19981201
US 1999-450691 A 19991130
WO 1999-US28306 W 19991201

AB A method of treating an affective disorder comprises administration of a (+)-venlafaxine derivative substantially free of the (-)-enantiomer. Thus, (±)-venlafaxine (preparation given) was added to a 0° mixture of Ph2PH and BuLi followed by stirring and reflux overnight to give 73.8% (±)-O-desmethylvenlafaxine, which was resolved to give (+)-O-desmethylvenlafaxine. Drug formulations containing the latter are given.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

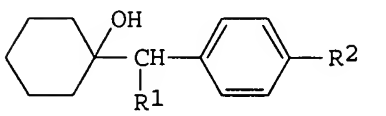
L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:81228 CAPLUS

CAS ONLINE PRINTOUT

DN 114:81228
TI Preparation of cyclohexanol derivatives as intermediates for antidepressants
IN Shepherd, Robin Gerald
PA John Wyeth and Brother Ltd., UK
SO Brit. UK Pat. Appl., 15 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | GB 2227743 | A1 | 19900808 | GB 1990-2095 | 19900130 |
| | GB 2227743 | B2 | 19920617 | | |
| | US 5043466 | A | 19910827 | US 1990-471187 | 19900126 |
| PRAI | GB 1989-2209 | A | 19890201 | | |

OS CASREACT 114:81228; MARPAT 114:81228
GI

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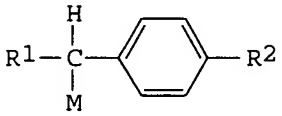
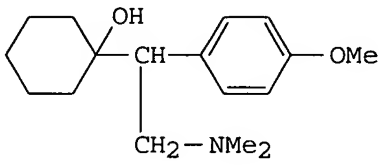



II

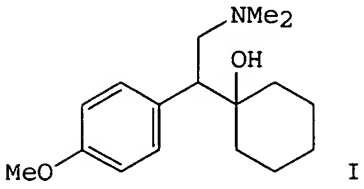



III

AB Title compds. I [R1 = cyano, CONMe2, CSNMe2; R2 = OMe, (protected) OH], useful as intermediates for preparation of antidepressants, were prepared by reaction of II [M = Li, Na, K, or MgX (X = halo); R2 = OMe, protected OH] with cyclohexanone in hydrocarbon/ether solvents. For example, II (R1 = CSNMe2, R2 = OMe, M = MgBr) gave the corresponding I in 64% yield. Subsequent reduction of I by Raney-Ni gave the antidepressant (no data) N,N-dimethyl-2-(1-hydroxycyclohexyl)-2-(4-methoxyphenyl)ethylamine (III).

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1990:630878 CAPLUS
DN 113:230878
TI 2-Phenyl-2-(1-hydroxycycloalkyl)ethylamine derivatives: synthesis and antidepressant activity
AU Yardley, John P.; Husbands, G. E. Morris; Stack, Gary; Butch, Jacqueline; Bicksler, James; Moyer, John A.; Muth, Eric A.; Andree, Terrance; Fletcher, Horace, III; et al.
CS Wyeth-Ayerst Res., Princeton, NJ, 08543-8000, USA
SO Journal of Medicinal Chemistry (1990), 33(10), 2899-905
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 113:230878
GI

CAS ONLINE PRINTOUT




I

AB A series of 2-phenyl-1-(1-hydroxycycloalkyl)ethylamine derivs. was examined for the ability to inhibit both rat brain imipramine receptor binding and the synaptosomal uptake of norepinephrine (NE) and serotonin (5-HT). Neurotransmitter uptake inhibition was highest for a subset of 2-phenyl-2-(1-hydroxycyclohexyl)dimethylethylamines in which the aryl ring has a halogen or methoxy substituent at the 3- and/or 4-positions. Potential antidepressant activity in this subset was assayed in three rodent models-the antagonism of reserpine-induced hypothermia, the antagonism of histamine-induced ACTH release, and the ability to reduce noradrenergic responsiveness in the rat pineal gland. An acute effect seen in the rat pineal gland with several analogs, including 1-[1-(3,4-dichlorophenyl)-2-(dimethylamino)ethyl]cyclohexanol and 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol (I), was taken as a possible correlate of a rapid onset of antidepressant activity. Compound I (venlafaxine) is presently undergoing clin. evaluation.

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1985:5895 CAPLUS
DN 102:5895
TI Phenethylamine derivatives and intermediates
IN Husbands, George Edward Morris; Yardley, John Patrick; Muth, Eric Anthony
PA American Home Products Corp., USA
SO Eur. Pat. Appl., 58 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 112669 | A2 | 19840704 | EP 1983-307435 | 19831207 |
| | EP 112669 | A3 | 19841128 | | |
| | EP 112669 | B1 | 19870729 | | |
| | R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE | | | | |
| | US 4535186 | A | 19850813 | US 1983-545701 | 19831026 |
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| | AU 567524 | B2 | 19871126 | | |
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| | GB 2133788 | A1 | 19840801 | GB 1983-32598 | 19831207 |
| | GB 2133788 | B2 | 19870715 | | |
| | AT 28628 | E | 19870815 | AT 1983-307435 | 19831207 |
| | FI 8304523 | A | 19840614 | FI 1983-4523 | 19831209 |
| | FI 77647 | B | 19881230 | | |
| | FI 77647 | C | 19890410 | | |
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| | DK 166372 | C | 19930906 | | |
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| | HU 199104 | B | 19900129 | | |
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| | ES 544402 | A1 | 19880401 | ES 1985-544402 | 19850531 |
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| | GB 2173787 | B2 | 19870715 | | |
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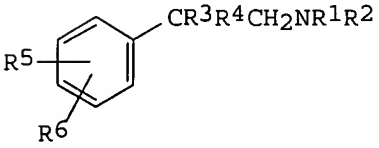
| PRAI | US 1982-449032 | A | 19821213 | | |
| | US 1983-486594 | A | 19830419 | | |
| | GB 1983-16646 | A | 19830618 | | |
| | US 1983-545701 | A | 19831026 | | |
| | EP 1983-307435 | A | 19831207 | | |
| | GB 1983-32598 | A3 | 19831207 | | |

OS CASREACT 102:5895; MARPAT 102:5895

GI




I

AB About 35 I [R1 = H, C1-6 alkyl; R2 = C1-6 alkyl; R3 = optionally unsatd. 1-hydroxycycloalkyl, optionally unsatd. 1-alkoxycycloalkyl, 1-cycloalkenyl; R4 = H, C1-6 alkyl; R5, R6 = H, OH, C1-6 alkyl, alkoxy, alkanoyloxy, -CN, NO2, alkylthio, NH2, alkylamino, dialkylamino, carboxamido, halo, CF3; R5R6 = methylenedioxy], antidepressants, were prepared E.g., p-MeOC6H4CH2CN in THF was treated with BuLi at -70°, then condensed with cyclohexanone at -50° to give 1-[cyano(p-methoxyphenyl)methyl]cyclohexanol (II). II was hydrogenated in NH3-EtOH over 5% Rh on Al2O3, then methylated with HCHO and HCO2H to give 1-[(2-dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol (III). III showed an activity equal to imipramine in synaptosomal NE and 5-HT uptake inhibition. Also, unlike the tricyclic antidepressants, III and related compds. demonstrate neither muscarinic anticholinergic activity nor antihistaminic activities.

=> FIL STNGUIDE

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 30.73 | 36.35 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -7.50 | -7.50 |

FILE 'STNGUIDE' ENTERED AT 08:57:12 ON 01 MAR 2006



FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 24, 2006 (20060224/UP).

CAS ONLINE PRINTOUT

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